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NCIC HPV
Sent by: Mary-Beth Weaver

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cc:
cc:
Subject: Environmental Defense comments on 2-Pyrrolidone (CAS# 616-45-5)

Richard_Denison@environmentaldefense.org on 06/02/2003 02:02:55 PM

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Subject: Environmental Defense comments on 2-Pyrrolidone (CAS# 616-45-5)

(Submitted via Internet 6/02/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and erauckman@charter.net)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for 2-Pyrrolidone (CAS# 616-45-5).

The test plan and robust summaries for 2-pyrrolidone (2-PO) were submitted by the 2-PO Consortium and were prepared by the Toxicology and Regulatory Affairs Group. Overall, the documents are informative and well-written. 2-PO has a very wide array of uses, including applications as a chemical intermediate, petroleum solvent, plasticizer, and ingredient in some pharmaceuticals and digital inks. Based on these applications, there are many opportunities for human and environmental exposures. It would be helpful if the sponsor provided information on the presence of 2-PO in industrial releases and additional data on the estimated or measured magnitude of human exposures from environmental or consumer sources.

The sponsor claims that existing data are adequate to fulfill requirements for all HPV endpoints. However, we do not fully agree and we recommend additional studies on the toxicity of 2-PO to aquatic invertebrates and algae. Additionally, there are some omissions in the robust summaries that raise questions regarding the adequacy of data for the reproductive toxicity endpoint. Specific comments are as follows:

1. Available data from experiments, estimations and the use of surrogates clearly indicate that 2-PO is readily biodegradable and that it should not accumulate in the environment.

2. Data presented in the robust summaries indicate that 2-PO has low acute toxicity, is not genotoxic and has low toxicity in repeat dose experiments with no apparent target organ.

3. Existing data on the toxicity to aquatic invertebrates and algae are inconsistent in that in both cases ECOSAR predictions are in dramatic conflict with experimental data. For example, ECOSAR predictions for Daphnia toxicity are 8733 mg/l whereas one experiment indicated and LD 50 of 13 mg/l. A similar wide disparity in ECOSAR predictions and experimental data occurred for algal toxicity. The sponsor has a plausible explanation for these findings based on the possibility that the 2-PO used in the experiments might have been contaminated with gamma butyrolactone, which is an intermediate in the synthesis of 2-PO. Gamma butyrolactone is highly toxic to both plants and aquatic invertebrates. However, the identities and levels of contaminants in the Z-PO experiments have not been indicated and

the algal experiments were conducted using a 2-PO sample that was 99.5% pure. For these reasons, we recommend that the sponsor conduct additional experiments on the toxicity of 2-PO to aquatic invertebrates and plants using a test substance subjected to rigorous chemical analysis.

4. The sponsor states that the existence of high-quality repeat dose and developmental toxicity studies showing no apparent effect on reproductive tract organs negates the need for a reproductive toxicity study. While we agree with this policy and the existing studies are certainly good studies, we reserve judgment at this time with respect to whether a reproductive toxicity study is needed, for the following two reasons. First, in cases where histological analysis of reproductive tract organs is used as a basis for negating the need for reproductive toxicity studies, we recommend that the list of reproductive tract tissues that were examined be listed in the robust summaries. Second, the test plan states that there are three existing developmental toxicity studies: two in rats using oral gavage were essentially negative, while the other using ip injection was apparently positive. The positive study was not made available in the robust summaries so we were not able to evaluate its quality. This study should be made available, although we do agree that the oral gavage route of exposure is a more relevant route of exposure for 2-PO.

Thank you for this opportunity to comment.

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